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Comparison of 810 nm and 1064 nm Wavelengths for Interstitial Laser Photocoagulation in Rabbit Brain

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Background and Objective: **This laboratory animal study is a comparison of Nd:YAG 1064 nm and diode 810 nm laser wavelengths in brain interstitial laser photocoagulation (ILP). Specific goals were to identify potential complications and physical characteristics of the thermal damage at both wavelengths prior to undertaking a clinical trial in humans.**
Study Design/Materials and Methods: **A total of 41 ILP illuminations were performed in vivo in the brains of 33 anesthetized rabbits using plane-cut fiber tips implanted directly or through catheters, and diffusing fiber tips. Delivered powers ranged from 1.1 to 4.2 W. Exposures ranged from 300 to 900 s. Survival ranged from 0 to 48 h. Experiments were performed in animals with and without VX-2 brain tumors.**
Results: **Thermal damage from 1.1 W at 810 nm was similar to that from 1.6 W at 1064 nm, but more pronounced. With plane-cut fiber tips, there was a greater propensity for severe physical effects (smoke, charring, bubbling, surface damage) at 810 nm than at 1064 nm, yet hemorrhage, thrombosis and vapor dissemination were observed at both wavelengths, in both normal brain and tumor.**
Conclusions: **For ILP in brain, 1064 nm may be better suited than 810 nm, although both are questionable with plane-cut-fiber tips. Compactness and portability may be the only valid reasons for using laser diodes operating around 810 nm. At 1064 nm, the power delivered from plane-cut fiber tips should be less than 1.5 W, necessitating long exposures, or else an open catheter should be used. Fiber tips with distributed emission may be preferred, provided structural integrity can be maintained. Lasers Surg. Med. 21:50–58, 1997** **© 1997 Wiley-Liss, Inc.**

Key words: interstitial laser photocoagulation (ILP); brain; Nd:YAG; laser diode

INTRODUCTION

Interstitial laser photocoagulation (ILP) is a form of minimally invasive cancer therapy in which continuous laser energy is delivered into a solid tumor volume through one or more implanted optical fibers. Most commonly, distributed heating of the entire tumor volume is attempted by delivering near-infrared laser energy from each fiber at a comparatively low power (1.5–2.5 W) and lengthy exposure (500–1000 s). Sufficient heating is achieved when tissue temperatures reach approximately 60°C, which results in thermal coagulative necrosis [1].

Clinically, ILP has been used to destroy unresectable tumors in brain [2,3], head and neck

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[4,5], and liver and pancreas [6–10]. ILP has the useful characteristic that thermally induced lesions can be visualized using real-time ultrasound, magnetic resonance imaging and possibly computerized tomography. For all sites, ILP is still considered experimental.

The optimal wavelength for ILP is unknown. ILP usually has been performed using a continuous Nd:YAG laser operating at 1064 nm because optical energy penetrates soft tissues well (3–8 mm) at this wavelength [11]. Maximal optical penetration produces minimal temperature gradients and, until recently, was believed to produce maximal thermal lesions. It is now known that when ILP is performed using a point optical source, the thermal lesion volume is increased by decreasing the optical penetration, but at the expense of increased smoke and vapor production [12,13].

Laser diodes operating near 800 nm are an attractive alternative source of optical power for ILP. They are more compact, portable and much cheaper than Nd:YAG lasers, and offer the advantage that multiple optical fibers can be excited and controlled independently with comparative ease. Although not yet investigated for brain ILP, laser diodes are being used clinically and in laboratory investigations of hepatic ILP [13,14].

The present study is a comparison of Nd:YAG 1064 nm and diode 810 nm laser wavelengths in brain ILP using a rabbit brain model. Specific goals were to identify potential complications and physical characteristics of the resulting thermal damage at both wavelengths prior to undertaking a clinical trial in human patients. Illumination parameters were allowed to evolve as the study progressed based on the observed complications. This study is observational and qualitative.

MATERIALS AND METHODS

A total of 41 ILP illuminations were performed in 33 mature New Zealand white rabbits, each weighing approximately 4 kg. Animals were cared for according to the Canadian Council for Animal Care Guidelines, under the purview of the Animal Research Ethics Board at McMaster University. Animals underwent general anesthesia through intramuscular injection with ketamine hydrochloride (50 mg/kg) and acepromazine maleate (1 mg/kg).

For all illuminations, an optical fiber (plastic-clad silica, 400 μm core diameter, 800 μm outer diameter) was inserted, following a small craniectomy, into the right or left cerebral hemisphere through the top of the skull, either directly or through a catheter (polyurethane, 2.1 mm inner diameter, PS Medical, Goleta, CA). Catheters with both open and closed ends were used. Open catheters were used to enable vapor to escape for several illuminations in which significant vapor production was anticipated. Each implant site was 5–10 mm lateral to the midline, 5–10 mm caudal to the fronto-parietal bone suture and 7–10 mm deep.

The delivered power was measured before each illumination using an external power meter (Ophir Model DG, Jerusalem). Reported powers are accurate to approximately ±0.1 W. Both plane-cut and diffusing fiber tips (PDT Systems Inc, San Jose, CA) were used. Plane-cut tips were cleaned, cleaved and polished before each illumination. Diffusing tips were not reused.

In 15 rabbits, VX-2 carcinoma acquired from local sources (see Acknowledgments) was seeded and grown at the intended treatment site for 14 days prior to treatment. In each case, 50 μl of saline containing approximately 5×10^5 viable tumor cells was injected slowly into the intended treatment site. The tumor cell suspensions were prepared as described by Zagzag et al. [15].

Survival time varied between 0 and 48 h post-illumination. Rabbits were killed by euthanyl injection, after which the brain was removed and fixed in 10% formalin for at least a week. The fixed brains were sliced serially in transverse planes (orthogonal to the fiber) at intervals of approximately 3 mm. Microscopic sections were prepared and stained with luxol-fast blue or hematoxylin and eosin for histopathological examination.

The illumination parameters specific to each wavelength are as follows.

Brain ILP at 1064 nm

A total of 27 illuminations were performed in the brains of 23 rabbits. These experiments are summarized in Table 1. Optical power from a continuous Nd:YAG laser operating at 1064 nm (Model C-100, CVI Laser Corp., Albuquerque, NM) was directed into each implanted optical fiber. Fourteen illuminations were performed in normal rabbit brain, 13 were performed in tumor-implanted sites.

Plane-cut fiber tips were used for 17 illuminations. In each of these, a power of at least 1.5 W was delivered [16]. Cylindrical diffusing tips of

TABLE 1. Illumination Parameters and Specific Observations for ILP in Rabbit Brain at 1064 nm

Illumination no.	Normal/ tumor	Technique vector[a]	Catheter (open/closed/ none)	Survival	Specific observations
1,2	Normal	4.2 and 3.0, 900, cyl. diffuser	None	0–2 h (acute)	Unremarkable
3,4	Normal	3.0 and 2.0, 900, cyl. diffuser	None	0–2 h (acute)	Unremarkable
5	Normal	2.0, 900, cyl. diffuser	None	48 h	Unremarkable
6,7	Normal	1.5, 900, point diffuser	None	0–2 h (acute)	One tip self-destroyed after 5 min
8,10	Normal	1.5, 900, point diffuser	None	died overnight	Unremarkable
9	Normal	1.5, 900, point diffuser	None	48 h	Unremarkable
11,12	Normal	1.5, 900, plane-cut	None	0–2 h (acute)	Charring on one tip post-illumination
13	Normal	2.5, 300, plane-cut	Closed	died overnight	Charring on catheter tip post-illumination
14	Normal	1.5, 500, plane-cut	Open	20 h euthanasia	Vapor plug rising in catheter
15–21	Tumor	1.6, 500, plane-cut	None	0–2 h (acute)	Transtentorial herniation
22	Tumor	2.5, 300, plane-cut	None	0–2 h (acute)	Surface bubbling
23–26	Tumor	1.7, 500, plane-cut	None	0–2 h (acute)	Surface bubbling
27	Tumor	1.6, 500, plane-cut	Closed	48 h	Unremarkable

[a]Power (W), exposure(s), fiber tip.

length 1.5 cm and point diffusing tips were each used for five illuminations, delivering powers based on available data from experiments in liver [17]. Unlike the 810 nm illuminations, it was not possible to monitor the 1064 nm illuminations with computerized tomography (CT) due to hospital restrictions on laser usage.

Brain ILP at 810 nm

A total of 14 illuminations were performed in the brains of 10 rabbits. These experiments are summarized in Table 2. The optical power source used was a fiber-coupled continuous laser diode operating at 810 ± 10 nm (Model LDT 27005-2F, Laser Diode Products Inc., New Brunswick, NJ) and delivering a maximum power of 2.0 W. It was possible to use plane-cut but not diffusing fiber tips because the laser diodes were manufactured pre-coupled to ordinary optical fiber. The delivered power initially was set to 1.6 W, as for the 1064 nm illuminations, but subsequently was lowered to 1.1 W (see Results).

It was possible to monitor eight illuminations with CT because the laser diodes were easily portable to a CT suite, although survival surgery was disallowed in these cases. As shown in Table 2, 12 illuminations were performed in normal rabbit brain and two were performed in tumor-implanted sites. (This imbalance arose because in four rabbits the implanted tumor cell suspensions failed to produce solid tumors.)

RESULTS

The rabbits reported here survived the illuminations (three rabbits not reported here died during anesthesia), although in several cases (see Tables 1,2) death occurred spontaneously within 1 h post-illumination. Herniation of brain through the craniectomy was frequently observed during or immediately after ILP. The effects of herniation were minimized by allowing expansion through a larger craniectomy site, and by administering dexamethazone post-illumination to rabbits intended to survive longer than 2 h. Specific observations arising during or after the illuminations are recorded in Tables 1 and 2. These and histopathological observations are discussed below.

Brain ILP at 1064 nm

The delivered power at 1064 nm was 1.5–2.5 W for all illuminations in which plane-cut fiber tips were implanted directly or through an open catheter. In most of these, charring was observed on the distal 2–3 mm of the fiber tip upon removal post-illumination, often supporting a 1–2 mm accretion of apparently necrotic tissue. Typically, vapor bubbles and smoke were observed intermittently at the fiber entry point on the brain surface. Bubbles comprising a "vapor plug" were observed rising up the open catheter in illumination no. 14.

As expected, smoke and vapor bubbles were not observed during the closed catheter illumination (no. 13) or during the 10 illuminations with cylindrical and point diffusing fiber tips. Charring was observed only as a 1 mm speck on the closed catheter tip upon removal post-illumination. Experiments with diffusing tips were discontinued

TABLE 2. Illumination Parameters and Specific Observations for ILP in Rabbit Brain at 810 nm

Illumination no.	Normal/tumor	Technique vector[a]	Catheter (open/closed/none)	Survival	Specific observations
1,5	Normal	1.6, 500, plane-cut	Closed	0–2 h (acute)	Catheters destroyed at brain surface
2	Normal	1.6, 500, plane-cut	None	0–2 h (acute)	Fiber tip repelled to brain surface
3,4	Normal	1.6, 500, plane-cut	None	0–2 h (acute)	Smoke, CT shows 2–4 mm defects
6	Normal	1.6, 500, plane-cut	None	0–2 h (acute)	Fiber destroyed at brain surface
7,8	Normal	1.1, 500, plane-cut	Fiber tip 2 mm beyond end of open catheter	0–2 h (acute)	Vapor plug rising continuously in catheter, catheter melted in one case
9,10	Normal	1.1, 500, plane-cut	Fiber tip 3 mm beyond end of open catheter	0–2 h (acute)	Vapor plug rising continuously in catheter
11,12	Normal	1.1, 500, plane-cut	Fiber tip 3 mm beyond end of open catheter	24 h	Vapor plug rising then stationary in catheter
13	Tumor	1.1, 500, plane-cut	None	0–2 h (acute)	Smoke, charring, CT shows 4–5 mm defects
14	Tumor	1.1, 500, plane-cut	None	0–2 h (acute)	Charring, CT shows substantial vapor production

[a]Power (W), exposure(s), fiber tip.

after illumination no. 10 because of their potential for thermal self-destruction at powers sufficient for clinical ILP, such as occurred in illumination no. 6 and as reported elsewhere during the course of this study [17].

Brain ILP at 810 nm

At 810 nm, all rabbits but one died within 1 h post-illumination, either spontaneously or because survival surgery was disallowed. After six illuminations, it became clear that 1.6 W was an excessive delivered power, in contrast to the 1064 nm illuminations. For non-catheterized plane-cut fiber tips, internal vapor pressure was sufficient to repel the implanted fiber tip to the brain surface, whereupon it generated substantial smoke and charring. In one case the fiber tip destroyed itself at the surface. In the two cases in which the non-catheterized fiber tip remained intact during ILP, CT images showed significant defects (dimension >2 mm), indicating substantial and remote internal vapor accumulation, as shown in Figure 1a. Both fiber tips implanted in closed catheters generated sufficient heat to melt the catheter.

The physical observations during and immediately after all eight illuminations with plane-cut fibers delivering 1.1 W were similar to those described for 1.5–1.7 W of 1064 nm energy (charring and accretion on fiber tip, smoke and vapor bubbles, vapor plugs rising up open catheters). A typical fiber tip and open catheter combination is shown post-illumination in Figure 2. The open catheter illuminations indicated that a plane-cut fiber tip should protrude approximately 3 mm beyond the catheter (less melts the catheter, more compromises vapor removal).

For ILP in VX-2 brain tumor at 810 nm and 1.1 W, CT images showed substantial vapor defects of dimension 4 mm and greater, similar to observations at 810 nm and 1.6 W. In one case (Figure 1b), substantial vapor accumulation was observed in a ventricle.

Histopathological Observations at 1064 nm and 810 nm

The ILP (thermal) lesions at 1064 nm were typical in appearance and are similar to those described previously [16,18]. Briefly, for plane-cut fiber tips, the center of the lesion typically is a defect of dimension 2–3 mm, circumscribed by caramelization, charring and vacuolation in cases where charring has occurred, as shown in Figure 3. This central defect is surrounded by thermal coagulative necrosis, comprising the main body of the lesion and most dense near the defect. Variable hemorrhage and thrombosis are observed throughout the coagulative necrosis. For diffusing fiber tips, charring and vacuolation are less common, provided the fiber tip remains patent.

The thermal lesion is sharply demarcated from surrounding normal tissue, although this demarcation is not evident on stained microscopic sections taken from animals surviving only a few hours post-illumination. By 24 h post-illumination an edema halo may be seen at the periphery

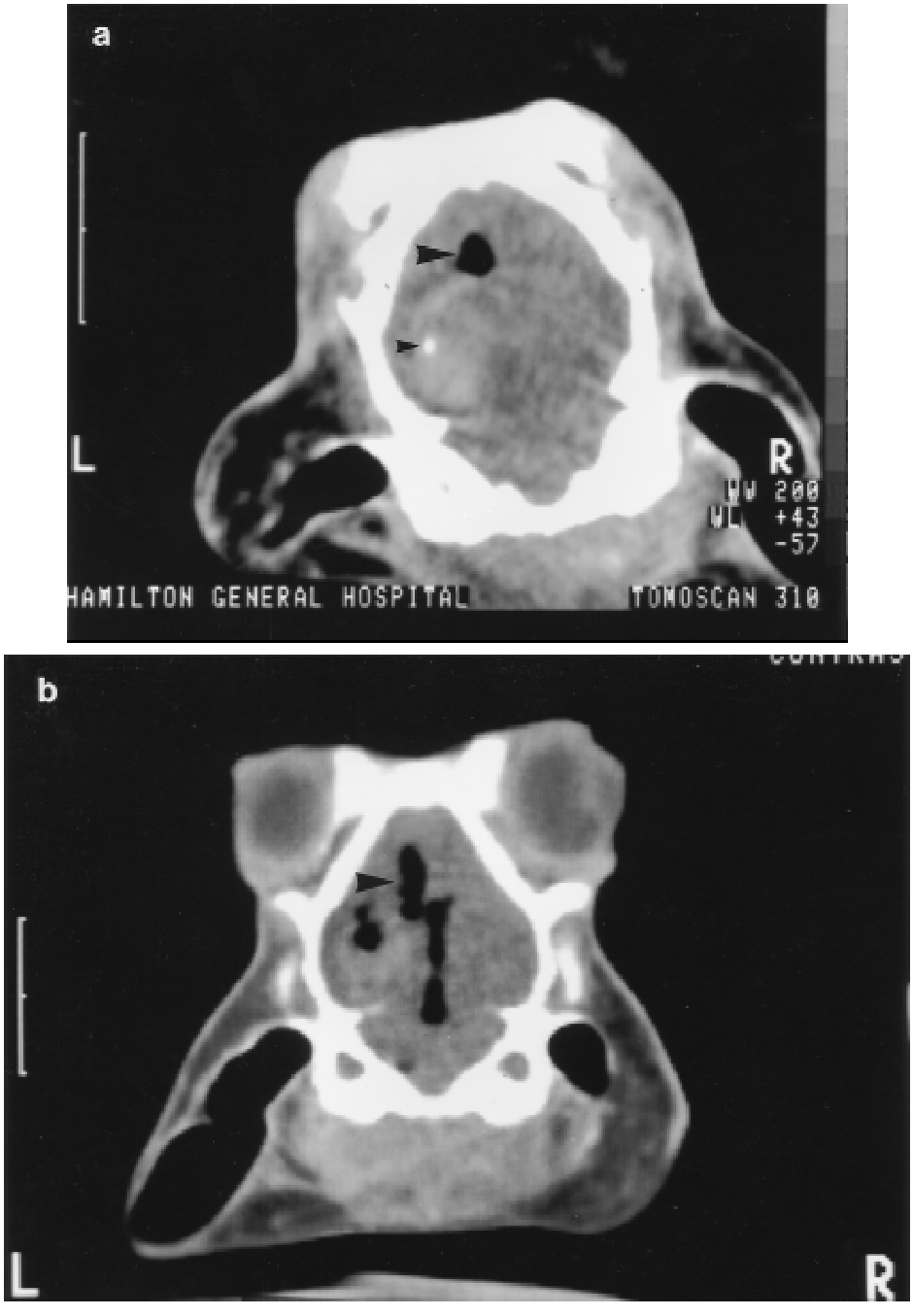

Fig. 1. CT images acquired during ILP at 810 nm in rabbit brain show significant defects (dimension >2 mm) representing vapor accumulation in ventricles (large arrowheads). A 2 cm scale is shown at left. The delivered power was **(a)** 1.6 W (normal brain—no. 3, Table 2) and **(b)** 1.1 W (brain tumor—no. 13, Table 2). The fiber tract (small arrowhead) is also evident in a. The thermal lesions are otherwise poorly imaged.

of the thermal lesion. As described previously, ILP thermal lesions in brain at 1.6 W are typically of dimension 10 ± 2 mm, depending on exposure duration [16].

The implanted VX-2 tumor cells grew to solid tumors of dimension 7 ± 2 mm over the 14-day growth period prior to ILP. The tumor was often irregular with perivascular extensions. In two "control" rabbits not listed in Table 1, VX-2 tumors were grown but ILP was not performed. In these cases, minimal necrosis was observed at the tumor core.

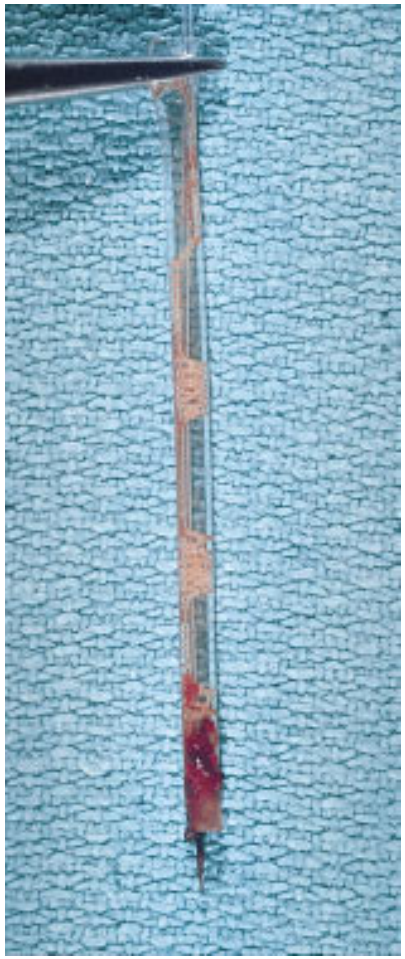

Fig. 2.

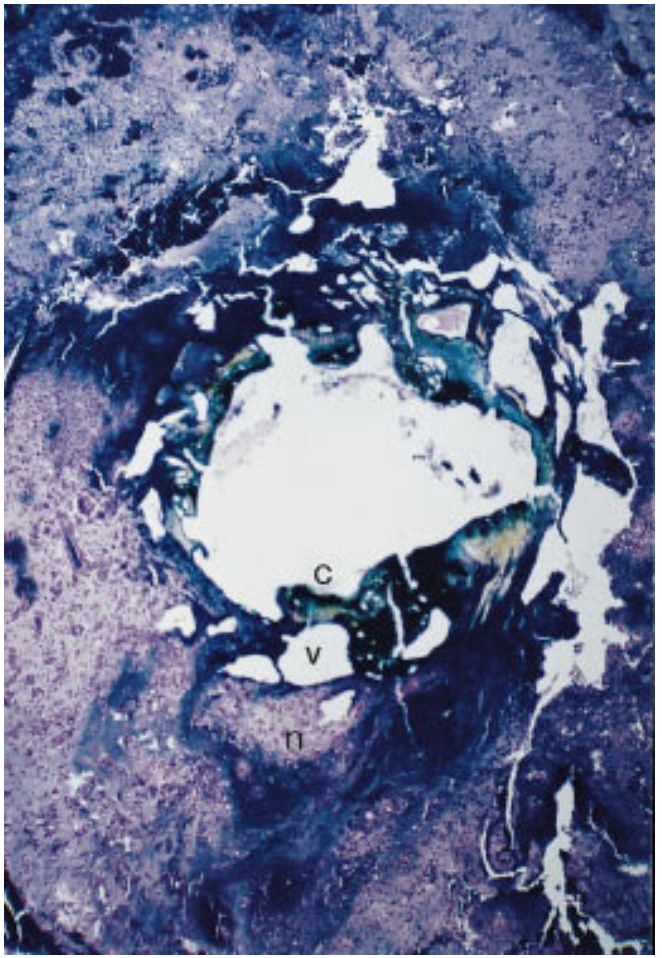

Fig. 3.

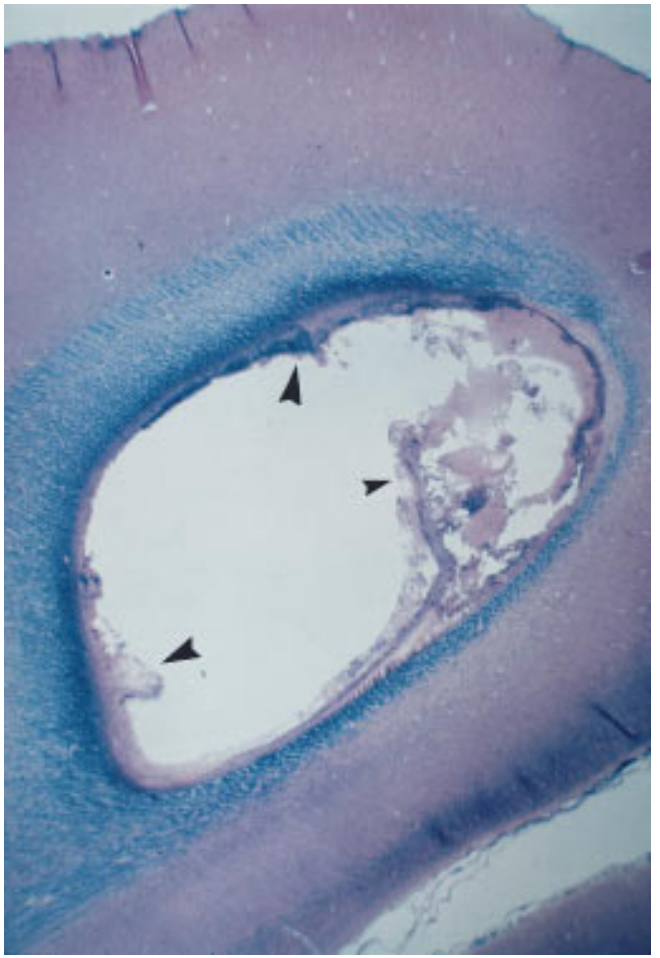

Fig. 4.

Legends to Figs. 2, 3, and 4 on following page.

Thermal damage from 1.1 W at 810 nm was similar to that described above for 1.6 W at 1064 nm, but more pronounced. Substantial vacuolation pockets, hemorrhage and thrombosis were observed outside the central defect in the 810 nm thermal lesions. Also, damage to ventricular ependymal lining was observed directly in three animals (may have occurred in others), suggesting dissemination of hot vapor within the ventricular system (Figure 4). This observation is consistent with the radiological observations described for 810 nm and shown in Figure 1.

DISCUSSION

The rabbit brain model is of limited validity for investigating clinical brain ILP because it is comparatively small. Typical thermal lesions of dimension 10 ± 2 mm occupy a substantial fraction of a rabbit's cerebrum.

The VX-2 tumor model is a common brain tumor model in rabbits and thus was used in these experiments. It is, however, of limited validity as a model for human brain tumors because VX-2 carcinoma cells disseminate more rapidly and extensively in the rabbit brain than both primary and metastatic tumors in the human brain.

During hepatic ILP, hyperechoic ultrasound images of thermal lesions are thought to be generated by dispersing microbubbles [19]. Vaporization is thus believed necessary for effective ultrasound monitoring, so that wavelengths less penetrating than 1064 nm may be useful. Brain ILP, by contrast, is monitored using CT or magnetic resonance imaging, and the role of vaporization in forming thermal lesion images is uncertain [16,20]. Vaporization, subsequent charring and other strong physical effects are of great relevance to ILP.

In this study, at both 1064 nm and 810 nm, the illumination parameters (delivered power, fiber tip type, catheterization) were allowed to vary in an attempt to determine clinically relevant parameters for a subsequent clinical trial in human patients. Given that ILP is an invasive physical therapy in brain, a single complication at any parameter setting was interpreted as necessitating a change of parameter(s). (For example, a single occurrence of a melted catheter suggests insufficiency.) This study is thus evolutional, not statistical.

Generally, these experiments indicate that, at both 810 nm and 1064 nm, there should be serious concern about performing clinical ILP in brain using plane-cut fiber tips. The CT images acquired during ILP at 810 nm with a plane-cut fiber tip delivering 1.1 W show clearly the propensity of this wavelength for generating substantial vapor internally. Although CT images could not be acquired during ILP at 1064 nm, the similarity of physical observations at 1064 nm (1.6 W) and 810 nm (1.1 W) suggests that internal vapor accumulation is likely also at 1064 nm (1.6 W).

It was possible for vapor produced near the fiber tip to be transported through the ventricular system, damaging ependymal lining. This unacceptable result raises questions about the likelihood/extent of vapor transport in the larger human brain, especially if the target volume is near a ventricle. Another concern is that, at both wavelengths, some degree of hemorrhage typically was observed in the main coagulation zone of the thermal lesions.

At a delivered power of 1.6 W, ILP with plane-cut fiber tips was feasible at 1064 nm but not at 810 nm due to catastrophic damage of the fiber and/or tissue at the brain surface. This difference of effect might be attributable to manufacturing differences in the optical fibers coupled to the different lasers, although both lasers' fibers were plastic-clad silica, 400 μm core diameter. More likely, the optical diffusion length in brain is less at 810 nm than at 1064 nm, as is true for liver [14].

With plane-cut fiber tips, a delivered power of 1.1 W at 810 nm produced physical effects (smoke, charring, bubbling) comparable in severity to those produced by 1.6 W at 1064 nm. In a clinical setting, the deliverable power presumably would be limited by these effects, so that thermal lesions could be made at higher power and there-

Fig. 2. A typical fiber tip and open catheter combination post-illumination (no. 7, Table 2), showing charring and accretion on fiber tip, and vapor plugs rising up the catheter.

Fig. 3. Microphotograph of a 1064 nm ILP lesion in a rabbit brain with tumor (no. 15, Table 1), obtained by staining a microscopic tissue section cut orthogonal to the implanted fiber with luxol fast blue. True magnification, ×200. The ILP lesion consists of a central defect of dimension 2–3 mm, circumscribed by vacuolation (v) and charring (c), and surrounded by thermal coagulative necrosis (n).

Fig. 4. Microphotograph showing damage to the ependymal lining of the lateral ventricle following 810 nm ILP in a rabbit brain tumor (no. 13, Table 2), obtained by staining a microscopic tissue section cut orthogonal to the implanted fiber with luxol fast blue. True magnification, ×80. Extended disruption of the ependymal layer (large arrowheads) and exudation of blood and fibrin into the ventricle (small arrowhead) are observed, corresponding to the radiologic observations in Figure 1b.

fore larger with 1064 nm energy than with 810 nm energy.

These experiments indicate that an open catheter may function effectively with plane-cut fiber tips as a vapor escape conduit, but the reliability of this mechanism appears to depend sensitively on implantation technique. In particular, a fiber tip protruding less than 3 mm beyond the end of catheter has proven capable of melting the catheter tip. Yet a protrusion distance much greater than 3 mm could place the catheter tip too far from the vapor source to collect vapor, or subject it to a vapor pressure too low for the vapor to traverse the coagulated tissue plug that typically accretes in the catheter tip (see Figure 2).

Diffusing-tipped fibers should be used only after reliability of their structural integrity has been checked at the delivered power to be used. Success has been reported using the ITT fiber tip [3], which is a nondiffusing axial emitter.

In summary, 1064 nm appears to be better suited for brain ILP than 810 nm, although both are questionable with plane-cut fiber tips. Compactness and portability may be the only valid reasons for using laser diodes operating around 810 nm in brain ILP. With plane-cut fiber tips, there is a lesser propensity for severe physical effects at 1064 nm than at 810 nm, yet the possibility for hemorrhage, thrombosis and dissemination of vapor exists at both wavelengths. Clinically, it would seem prudent to conduct ILP using open catheters as vapor escape conduits, accepting the increase in implant diameter. Further assessment of catheter reliability is required. Delivered powers less than 1.5 W and longer exposures may be preferred for brain ILP. The best strategy may be to use fiber tips with distributed emission (diffusing or axial emitters). Rigorous wavelength comparisons should be undertaken for any delivery system before using it in a human clinical trial.

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REFERENCES

1. Thomsen S. Pathologic analysis of photothermal and photomechanical effects of laser-tissue interaction. Photochem Photobiol 1991; 53:825–835.
2. Roux FX, Merienne L, Leriche B, Lucerna S, Turak B, Devaux B, Chodkiewicz JP. Laser interstitial thermotherapy in stereotactical neurosurgery. Lasers Med Sci 1992; 7:121–126.
3. Schrottner O, Ascher PW, Ebner F. Interstitial laser thermotherapy of brain tumours under MRI control. Abstract C-24, Fifth International Congress of the European Laser Association, Graz, Austria, 1990.
4. Castro DJ, Lufkin RB, Saxton RE, Nyerges A, Schiller V, Grant E, Soudant J, Szaley M, Ward PH. MRI and/or ultrasound guided interstitial Nd:YAG laser phototherapy for palliative treatment of recurrent head and neck tumors: Clinical experience. Lasers Surg Med 1992; Suppl. 4:48.
5. Ohyama M, Nobori T, Moriyama I, Furuta S, Shima T. Laserthermia on head and neck malignancies: Experimental and clinical studies. Acta Otolaryngol 1988; Suppl. 458:7–12.
6. Amin Z, Donald JJ, Masters A, Kant R, Steger AC, Bown SG, Lees WR. Hepatic metastases: Interstitial laser photocoagulation with real-time US monitoring and dynamic CT evaluation of treatment. Radiology 1993; 187:339–347.
7. Steger AC, Lees W, Walmsley K, Bown SG. Interstitial laser hyperthermia: A new approach to local destruction of tumours. Br Med J 1989; 299:362–365.
8. Hahl J, Haapiainen R, Ovaska J, Puolakkainen P, Schoder T. Laser-induced hyperthermia in the treatment of liver tumours. Lasers Surg Med 1990; 10:319–321.
9. Dowlatshahi K, Bhattacharya AK, Silver B, Matalon T, Williams JW. Percutaneous interstitial laser therapy of a patient with recurrent hepatoma in a transplanted liver. Surgery 1992; 112:603–606.
10. Nolsoe CP, Torp-Pedersen S, Burcharth F, Horn T, Pedersen S, Christensen NH, Olldag ES, Andersen PH, Karstrup S, Lorentzen T, Holm HH. Interstitial hyperthermia of colorectal liver metastases with a US-guided Nd-YAG laser with a diffuser tip: A pilot clinical study. Radiology 1993; 187:333–337.
11. Svaasand LO. Dosimetry for laser-induced hyperthermia. Lasers Med Sci 1989; 4:309–315.
12. Wyman D, Wilson B, Adams K. Dependence of laser photocoagulation on interstitial delivery parameters. Lasers Surg Med 1994; 14:59–64.
13. Amin Z, Buonaccorsi G, Mills T, Harries S, Lees WR, Bown SG. Interstitial laser photocoagulation: Evaluation of a 1320 nm Nd-YAG and an 805 nm diode laser: The significance of charring and the value of precharring the fiber tip. Lasers Med Sci 1993; 8:113–120.
14. Jacques SL, Rastegar S, Motamedi M, Thomsen SL, Schwartz J, Torres J, Mannonen I. Liver photocoagulation with diode laser (805 nm) vs. Nd:YAG laser (1064 nm). SPIE Proceedings, Laser-Tissue Interactions III, Vol. 1646, Los Angeles, 1992.
15. Zagzag D, Brem S, Robert F. Neovascularization and tumor growth in the rabbit brain. Am J Pathol 1988; 131: 361–372.
16. Tracz RA, Wyman DR, Little PB, Towner RA, Stewart WA, Schatz SW, Pennock PW, Wilson BC. Magnetic reso-

nance imaging of interstitial laser photocoagulation in brain. Lasers Surg Med 1992; 12:165–173.
17. Malone DE, Wyman DR, Moote DJ, Mori H, Lewis R, DeNardi F, Swift CL, Wilson BC. Sonographic changes during hepatic interstitial laser photocoagulation: An investigation of 3 fiber tips. Invest Radiol 1992; 27:804–813.
18. Schatz SW, Bown SG, Wyman DR, Groves JT, Wilson BC. Low power interstitial Nd-YAG laser photocoagulation in normal rabbit brain. Lasers Med Sci 1992; 7:434–439.
19. Malone DE, Wyman DR, DeNardi FG, McGrath FP, deGara CJ, Wilson BC. Hepatic interstitial laser photocoagulation: An investigation of the relationship between acute thermal lesions and their sonographic images. Invest Radiol 1994; 29:915–921.
20. Bleier AR, Jolesz FA, Cohen MS, Weisskoff RM, Dalcanton JJ, Higuchi N, Feinberg DA, McKinstry RC, Hushek SJ. Real time magnetic resonance imaging of laser-tissue interactions. Magn Reson Med 1991; 21:132–137.